

Figure 1

1 GGAAGTCAGCAGCGTTGGGAGGGGTGGCGGGGGAATAGCGGGCAGC
51 AGCCCCAGCCCTCAGAGACAGACAGAAAGGAGGGAGGGTGCTGG
101 GGGACAGCCCCCACCATTCCCTACCGCTATGGGCCCAACCTCCACTCC
151 CACCTCCCCCTCCATCGGCCGGGCTAGGACACCCCAATCCGTCGCC
201 CCTTGGCACCGACACCCCGACAGACAGACAGCCATCCGCCACCA
251 CCGTGCCCGCAGCCTGGCTGGGAGGGGCCAGCCCCCAGCCCCCTAC
301 CCCTCTGAGGTGGCCAGA ATG GAT TTG TGG CCA GGG GCA TGG
Met Asp Leu Trp Pro Gly Ala Trp
343 ATG CTG CTG CTG CTC TTC CTG CTG CTG CTC TTC C
Met Leu Leu Leu Leu Phe Leu Leu Leu Phe L
10 20
380 TG CTG CCC ACC CTG TGG TTC TGC AGC CCC AGT GCC AAG
eu Leu Pro Thr Leu Trp Phe Cys Ser Pro Ser Ala Lys

Figure 1 (continued)

418 TAC TTC TTC AAG ATG GCC TTC TAC AAT GGC TGG ATC C
Tyr Phe Phe Lys Met Ala Phe Tyr Asn Gly Trp Ile L

40

455 TC TTC CTG GCT GTG CTC GCC ATC CCT GTG TGT GCC GTG
eu Phe Leu Ala Val Leu Ala Ile Pro Val Cys Ala Val

50

493 CGA GGA CGC AAC GTC GAG AAC ATG AAG ATC TTG CGT C
Arg Gly Arg Asn Val Glu Asn Met Lys Ile Leu Arg L

60

70

530 TA ATG CTG CTC CAC ATC AAA TAC CTG TAC GGG ATC CGA
eu Met Leu Leu His Ile Lys Tyr Leu Tyr Gly Ile Arg

80

Figure 1 (continued)

568 GTG GAG GTG CGA GGG GCT CAC CAC TTC CCT CCC TCG C
Val Glu Val Arg Gly Ala His His Phe Pro Pro Ser G

90

605 AG CCC TAT GTT GTT GTC TCC AAC CAC CAG AGC TCT CTC
In Pro Tyr Val Val Val Ser Asn His Gln Ser Ser Leu

100

643 GAT CTG CTT GGG ATG ATG GAG GTA CTG CCA GGC CGC T
Asp Leu Leu Gly Met Met Glu Val Leu Pro Gly Arg C

110

120

680 GT GTG CCC ATT GCC AAG CGC GAG CTA CTG TGG GCT GGC
ys Val Pro Ile Ala Lys Arg Glu Leu Leu Trp Ala Gly

130

Figure 1 (continued)

718 TCT GCC GGG CTG GCC TGC TGG CTG GCA GGC ATC T
Ser Ala Gly Leu Ala Cys Trp Leu Ala Gly Val Ile P
140

755 TC ATC GAC CGG AAG CGC ACG GGG GAT GCC ATC AGT GTC
he Ile Asp Arg Lys Arg Thr Gly Asp Ala Ile Ser Val
150

793 ATG TCT GAG GTC GCC CAG ACC CTG CTC ACC CAG GAC G
Met Ser Glu Val Ala Gln Thr Leu Leu Thr Gln Asp V
160 170

830 TG AGG GTC TGG GTG TTT CCT GAG GGA ACG AGA AAC CAC
al Arg Val Trp Val Phe Pro Glu Gly Thr Arg Asn His
180

Figure 1 (continued)

868 AAT GGC TCC ATG CTG CCC TTC AAA CGT GGC GCC TTC C
Asn Gly Ser Met Leu Pro Phe Lys Arg Gly Ala Phe H

190

905 AT CTT GCA GTG CAG GCC CAG GTT CCC ATT GTC CCC ATA
is Leu Ala Val Gln Ala Gln Val Pro Ile Val Pro Ile

200

943 GTC ATG TCC TCC TAC CAA GAC TTC TAC TGC AAG AAG G
Val Met Ser Ser Tyr Gln Asp Phe Tyr Cys Lys Lys G

210

220

980 AG CGT CGC TTC ACC TCG GGA CAA TGT CAG GTG CGG GTG
lu Arg Arg Phe Thr Ser Gly Gln Cys Gln Val Arg Val

230

Figure 1 (continued)

1018 CTG CCC CCA GTG CCC ACG GAA GGG CTG ACA CCA GAT G
Leu Pro Pro Val Pro Thr Glu Gly Leu Thr Pro Asp A

240

1055 AC GTC CCA GCT CTG GCT GAC AGA GTC CGG CAC TCC ATG
sp Val Pro Ala Leu Ala Asp Arg Val Arg His Ser Met

250

1093 CTC ACT GTT TTC CGG GAA ATC TCC ACT GAT GGC CGG G
Leu Thr Val Phe Arg Glu Ile Ser Thr Asp Gly Arg G

260

270

1130 GT GGT GGT GAC TAT CTG AAG AAG CCT GGG GGC GGT GGG
ly Gly Gly Asp Tyr Leu Lys Lys Pro Gly Gly Gly 280

1168 TGA ACCCTGGCTCTGAGCTCTCCTCCCATCTGTCCCATCTTCTCTCCC

1216 CACACCTACCCAGTGGGCCCTGAAGCAGGGCCAAACCCCTTCTCCTT

1266 GTCTCCCCTCTCCCCTTATCTCCTCTTTTGGAATCTTCAACTTCTGAA

Figure 1 (continued)

1316 GTGAATGTGGATACAGCGCCACTCCTGCCCCCTCTTGGCCCCCATCCATGG
1366 ACTCTTGCCCTCGGTGCAGTTTCCACTCTTGACCCCCCACCCTCCTACTGTCT
1416 TGTCTGTGGACAGTTGCCCTCCCCCTCATCTCCAGTGACTCAGCCTACAC
1466 AAGGAGGGGAACATTCCATCCCCCAGTGGAGTCTCTTCCCTATGTGGTCTT
1516 CTC TACCCCTCTACCCCCACATTGGCCAGTGGACTCATCCATTCTTTGGA
1566 ACAAAATCCCCCCTCACTCCAAGTCCATGGATTCAATGGACTCATCCATT
1616 TGTGAGGAGGACTTCTCGCCCTCTGGCTGGAAGCTGATACCTGAAGCACT
1666 CCCAGGCTCATCCTGGGAGCTTTCCCTCAGCACCTTCACCTTCCCCTCCCAG
1716 TGTAGCCCTCCTGT CAGTGGGGCTGGACCCCTTCTAATTCAGAGGTCTCAT
1766 GCCTGCCCTTGCCCCAGATGCCCCAGGGTCGTGCACCTCTCTGGGATACCAGT
1816 TCAGTCTCCACATTCTGTGGTTTCTGTCCCCCATAGTACAGTTCTTCAGTG
1866 GACATGACCCCAAGCCAGCCCCCTGCAGCCCCCTGCTGACCATCTCACCAGAC
1916 ACAAGGGGAAGAAGCAGACATCAGGTGCTGCACCTCACTTCTGCCCCCTGG
1966 GGAGTTGGGAAAGGAACGAACCTGGCTGGAGGGGATAGGAGGGCTTTT

Figure 1 (continued)

2016 AATTATTTCTTTTCTGTGAGGCTTCCCCCTCTCTGAGCCAGTTTTC
2066 TTTCTTCCCTGGTGGCATTAGCCACTCCCTGCCCTCTCACTCCAGACCTGTT
2116 CCCACAAC TGGGAGGTAGGCTGGGAGCAAAAGGAGAGGGTGGGACCCAG
2166 TTTTGGCGTGGTGGTTTATTATTAATCTGGATAACAGCAAAAAAATG
2216 AAAATAAGAGAGAGAGAAAAA

Figure 2

Human LPAAT	1	MDLWPGAWM-	10	20	30	40	50
Yeast LPAAT	1	MSV-IGRFLY	----LLLLLF	LL-LLFLLPT	LWFCSPSAKY	F-----FKMA	
E.coli LPAAT	1	M-----	YLRSVL-VVL	AL-AG-----	---C-----	-----G	
Maize LPAAT	1	MAI-----	-----LYIF	RL-IITVIYS	ILVCVFGSIY	-----	
			---PLVLVVL	PLGLLFLLSG	LIVNAIQAVL	FVTIRPFESKS	
Human LPAAT	51	FYNGWILFLA	60	70	80	90	100
Yeast LPAAT	51	FY-----G	VLAIPVCAVR	GRNVENMKIL	RLMLLHIKYL	-YGIRVEVRG	
E.coli LPAAT	51	-----	VIASILCTLI	GKQHLAQWIT	ARCFYHVMKL	MLGLDV---K	
Maize LPAAT	51	FYRRINRFLA	EL-----	PRNPKHVATF	GHMFGRLAPL	-FGLKVECRK	
				-----L	WLQLVWVVDW	WAGVKVQLHA	
Human LPAAT	101	AHMF-PPSQ-	110	120	130	140	150
Yeast LPAAT	101	VVGE-ENLAK	KPYIMIANHQ	SSLDLIGMME	VL--PGRC--	-VPI-AKREL	
E.coli LPAAT	101	PTDA-ESYG-	-NAIYIANHQ	STLDIFMLGR	IF--PPGCT-	---VTAKKSL	
Maize LPAAT	101	DEETYRSMGK	EHALIISNHR	NNYDMVTASN	IVQ-PP----	TVTV-GKKSL	
				SDIDWL-IGW	ILAQRSGCLG	STLAVMKKSS	
Human LPAAT	151	LWAGSAGLAC	160	170	180	190	200
Yeast LPAAT	151	KYVPFLG---	W---LAGVIF	IDRKRTGDAL	SVMSEVAQTL	LTQDVRVWV-	
E.coli LPAAT	151	LWIPFFGQLY	W---LTGNLL	LDRSKRQEA	DTLNKGLENV	KKNKRALWV-	
Maize LPAAT	151	KFLPVIWISM	WF---AEYLF	IDRNNRTKAH	GTIAEVVNHF	KKRRI SIWM-	
				LERS-WAKDE	KTLKWGLQRL	KDFPRPFWLA	
Human LPAAT	201	FPEGTRNHN	210	220	230	240	250
Yeast LPAAT	201	FPEGTRSYT	GS-----	-----	MLPFKRGAFH	LAVQAQVPIV	
E.coli LPAAT	201	FPEGTRSRG	SEL-----	-----T	MLPFKKGAFH	LAQQKIPIV	
Maize LPAAT	201	LFVEGTRFTP	RGL-----	-----	-LPFKTGAFH	AAIAAGVPII	
				ASQGLPAPRN	VLIPTKGFV	SAVSIMRDFV	

Figure 2 (continued)

		260	270	280	290	300
Human LPAAT	251	<u>P</u> <u>I</u> <u>V</u> <u>M</u> <u>S</u> <u>S</u> <u>Y</u> <u>Q</u> <u>D</u> <u>F</u>	<u>Y</u> <u>C</u> <u>K</u> <u>E</u> <u>R</u> <u>R</u> <u>F</u> <u>T</u> <u>S</u>	<u>G</u> <u>Q</u> <u>C</u> <u>Q</u> <u>V</u> <u>R</u> <u>V</u> <u>L</u> <u>P</u> <u>P</u>	<u>V</u> <u>P</u> <u>T</u> <u>E</u> <u>G</u> <u>L</u> <u>T</u> <u>P</u> <u>D</u> <u>D</u>	<u>V</u> <u>P</u> <u>A</u> <u>L</u> <u>A</u> <u>D</u> <u>R</u> ---
Yeast LPAAT	251	<u>P</u> <u>V</u> <u>V</u> <u>S</u> <u>N</u> <u>T</u> <u>S</u> <u>T</u> <u>L</u>	<u>V</u> <u>S</u> <u>P</u> <u>K</u> <u>Y</u> <u>G</u> <u>V</u> <u>F</u> <u>N</u> <u>R</u>	<u>G</u> <u>C</u> <u>M</u> <u>I</u> <u>V</u> <u>R</u> <u>I</u> <u>L</u> <u>K</u> <u>P</u>	<u>I</u> <u>S</u> <u>T</u> <u>E</u> <u>N</u> <u>L</u> <u>T</u> <u>K</u> <u>D</u> <u>K</u>	<u>I</u> <u>G</u> <u>E</u> <u>F</u> <u>A</u> <u>E</u> <u>K</u> ---
E.coli LPAAT	251	<u>P</u> <u>V</u> <u>C</u> <u>V</u> <u>S</u> <u>T</u> <u>S</u> <u>N</u> <u>K</u>	<u>I</u> --- <u>N</u> <u>L</u> <u>N</u> <u>R</u> <u>L</u> <u>H</u> <u>N</u>	<u>G</u> <u>L</u> <u>V</u> <u>I</u> <u>V</u> <u>E</u> <u>M</u> <u>L</u> <u>P</u> <u>P</u>	<u>I</u> <u>D</u> <u>V</u> <u>S</u> <u>Q</u> <u>Y</u> <u>G</u> <u>K</u> <u>D</u> <u>Q</u>	<u>V</u> <u>R</u> <u>E</u> <u>L</u> <u>A</u> <u>A</u> <u>H</u> ---
Maize LPAAT	251	<u>P</u> <u>A</u> <u>I</u> <u>Y</u> <u>D</u> <u>T</u> --- <u>V</u>	<u>I</u> <u>V</u> <u>P</u> <u>K</u> <u>D</u> <u>S</u> <u>P</u> <u>Q</u> <u>P</u> <u>T</u>	<u>M</u> <u>L</u> <u>R</u> <u>I</u> <u>L</u> <u>K</u> <u>G</u> <u>Q</u> <u>S</u> <u>S</u>	<u>V</u> <u>I</u> <u>H</u> <u>V</u> <u>R</u> <u>M</u> <u>K</u> <u>R</u> <u>H</u> <u>A</u>	<u>M</u> <u>S</u> <u>E</u> <u>M</u> <u>P</u> <u>K</u> <u>S</u> <u>D</u> <u>E</u> <u>D</u>
		310	320	330	340	350
Human LPAAT	301	-----	<u>V</u> <u>R</u> <u>H</u> <u>S</u> <u>M</u> <u>L</u> <u>T</u> <u>V</u> - <u>F</u>	<u>R</u> <u>E</u> <u>I</u> <u>S</u> <u>T</u> <u>D</u> <u>G</u> <u>R</u> <u>G</u> <u>G</u>	<u>G</u> <u>D</u> <u>Y</u> <u>L</u> <u>K</u> <u>K</u> <u>P</u> <u>G</u> <u>G</u>	<u>G</u> *-----
Yeast LPAAT	301	-----	<u>V</u> <u>R</u> <u>D</u> <u>Q</u> <u>M</u> <u>V</u> <u>D</u> <u>T</u> - <u>L</u>	<u>K</u> <u>E</u> <u>I</u> <u>G</u> <u>Y</u> <u>S</u> <u>P</u> <u>A</u> <u>I</u> <u>N</u>	<u>D</u> <u>T</u> <u>T</u> <u>L</u> <u>P</u> <u>P</u> <u>Q</u> ---	-----
E.coli LPAAT	301	-----	<u>C</u> <u>R</u> <u>S</u> <u>I</u> <u>M</u> <u>E</u> <u>Q</u> <u>K</u> - <u>I</u>	<u>A</u> <u>E</u> <u>L</u> <u>D</u> <u>K</u> <u>E</u> <u>V</u> <u>A</u> <u>E</u> -	---- <u>R</u> <u>E</u> <u>A</u> <u>A</u> <u>G</u> <u>K</u>	<u>V</u> *-----
Maize LPAAT	301	<u>V</u> <u>S</u> <u>K</u> <u>W</u> <u>C</u> <u>K</u> <u>D</u> <u>I</u> <u>F</u> <u>V</u>	<u>A</u> <u>K</u> <u>D</u> <u>A</u> <u>L</u> <u>L</u> <u>D</u> <u>K</u> <u>H</u> <u>L</u>	<u>A</u> <u>T</u> <u>G</u> <u>T</u> <u>F</u> <u>D</u> <u>E</u> <u>E</u> <u>I</u> <u>R</u>	<u>P</u> <u>I</u> <u>G</u> <u>R</u> <u>P</u> <u>V</u> <u>K</u> <u>S</u> <u>L</u> <u>L</u>	<u>V</u> <u>T</u> <u>L</u> <u>F</u> <u>W</u> <u>S</u> <u>C</u> <u>L</u> <u>L</u> <u>L</u>
		360	370	380	390	400
Human LPAAT	351
Yeast LPAAT	351	-- <u>A</u> <u>I</u> <u>E</u> <u>Y</u> --- <u>A</u>	<u>A</u> <u>L</u> ----- <u>Q</u>	<u>H</u> <u>D</u> <u>K</u> <u>K</u> <u>V</u> <u>N</u> <u>K</u> <u>K</u> <u>I</u> <u>K</u>	<u>N</u> <u>E</u> <u>P</u> <u>V</u> <u>P</u> <u>S</u> <u>V</u> <u>S</u> <u>I</u> <u>S</u>	<u>N</u> <u>D</u> <u>V</u> <u>N</u> <u>T</u> <u>H</u> <u>N</u> <u>E</u> <u>G</u> <u>S</u>
E.coli LPAAT	351
Maize LPAAT	351	<u>F</u> <u>G</u> <u>A</u> <u>I</u> <u>E</u> <u>F</u> <u>F</u> <u>K</u> <u>W</u> <u>T</u>	<u>Q</u> <u>L</u> <u>L</u> <u>S</u> <u>T</u> <u>W</u> <u>R</u> <u>G</u> <u>V</u> <u>A</u>	<u>F</u> <u>T</u> <u>A</u> <u>A</u> <u>G</u> <u>M</u> <u>A</u> <u>L</u> <u>V</u> <u>T</u>	<u>G</u> <u>V</u> <u>M</u> <u>H</u> <u>V</u> <u>F</u> <u>I</u> <u>M</u> <u>F</u> <u>S</u>	<u>Q</u> <u>A</u> ----- <u>E</u> <u>R</u> <u>S</u>
		410	420	430	440	450
Human LPAAT	401
Yeast LPAAT	401	<u>S</u> ----- <u>V</u>	<u>K</u> <u>K</u> <u>M</u> <u>H</u> *
E.coli LPAAT	401
Maize LPAAT	401	<u>S</u> <u>S</u> <u>A</u> <u>R</u> <u>A</u> <u>A</u> <u>R</u> <u>N</u> <u>R</u> <u>V</u>	<u>K</u> <u>K</u> <u>E</u> *

Figure 3

10	20	30	40	50	60
GGAGCGAGCT	GGCGGCGCCG	TCGGGCGCCG	GGCCGGGCCA	TGGAGCTGTG	GCCGTGTCTG
70	80	90	100	110	120
GCCGCGGCGC	TGCTGTTGCT	GCTGCTGCTG	GTGCAGCTGA	GCCGCGCGGC	CGAGTTCTAC
130	140	150	160	170	180
GCCAAGGTCTG	CCCTGTACTG	CGCGCTGTGC	TTCACGGTGT	CCGCCGTGGC	CTCGCTCGTC
190	200	210	220	230	240
TGCCTGCTGT	GCCACGGCGG	CCGGACGGTG	GAGAACATGA	GCATCATCGG	CTGGTTCTGTG
250	260	270	280	290	300
CGAAGCTTCA	AGTACTTTTA	CGGGCTCCGC	TTCGAGGTGC	GGGACCCGCG	CAGGCTGCAG
310	320	330	340	350	360
GAGGCCCGTC	CCTGTGTTCAT	CGTCTCCAAC	CACCAGAGCA	TCCTGGACAT	GATGGGCCCTC
370	380	390	400	410	420
ATGGAGGTCC	TTCCGGAGCG	CTGCGTGCAG	ATCGCCAAGC	GGGAGCTGCT	CTTCCTGGGG
430	440	450	460	470	480
CCCGTGGGCC	TCATCATGTA	CCTCGGGGGC	GTCTTCTTCA	TCAACCGGCA	GCGCTCTAGC
490	500	510	520	530	540
ACTGCCATGA	CAGTGATGGC	CGACCTGGGC	GAGCGCATGG	TCAGGGAGAA	CCTCAAGATG

Figure 3 (continued)

550	560	570	580	590	600
TGGATCTATC	CCGAGGGTAC	TCGCAACGAC	AATGGGGACC	TGCTGCCCTTT	TAAGAAGGGC
610	620	630	640	650	660
GCCTTCTACC	TGGCAGTCCA	GGCACAGGTG	CCCATCGTCC	CCGTGGTGTA	CTCTTCCTTC
670	680	690	700	710	720
TCCTCCTTCT	ACAACACCAA	GAAGAACTTC	TTCACTTCAG	GAACAGTCAC	AGTGCAGGTG
730	740	750	760	770	780
CTGGAAGCCA	TCCCCACCCAG	CGGCCTCACT	GCGGCGGACG	TCCCTGCGCT	CGTGGACACC
790	800	810	820	830	840
TGCCACCCGG	CCATGAGGAC	CACCTTCCTC	CACATCTCCA	AGACCCCCCA	GGAGAACGGG
850	860	870	880	890	900
GCCACTGCGG	GGTCTGGCGT	GCAGCCGGCC	CAGTAGCCCA	GACCACGGCA	GGGCATGACC
910	920	930	940	950	960
TGGGGAGGGC	AGGTGGAAGC	CGATGGCTGG	AGGATGGCA	GAGGGGACTC	CTCCCCGGCTT
970	980	990	1000	1010	1020
CCAAATACCA	CTCTGTCCGG	CTCCCCCAGC	TCTCACTCAG	CCCCGGGAAGC	AGGAAGCCCC
1030	1040	1050	1060	1070	1080
TTCTGTCACT	GGTCTCAGAC	ACAGGCCCTT	GGTGTCCCCT	GCAGGGGGCT	CAGCTGGACC

Figure 3 (continued)

1090	1100	1110	1120	1130	1140
CTCCCCGGC	TCGAGGGCAG	GGACTCGGC	CCACGGCACC	TCTGGNGCT	GGGNTGATAA
1150	1160	1170	1180	1190	1200
AGATGAGGCT	TGCGGCTGTG	GCCCCGTGGT	GGGCTGAGCC	ACAAGGCCCC	CGATGGCCCA
1210	1220	1230	1240	1250	1260
GGAGCAGATG	GGAGGACCCC	GAGGCCAGGA	GTCCCAGACT	CACGCACCCT	GGGCCACAGG
1270	1280	1290	1300	1310	1320
GAGCCGGGAA	TCGGGGCCTG	CTGCTCCTGC	TGGCCTGAAG	AATCTGTGGG	GTCAGCCTG
1330	1340	1350	1360	1370	1380
TACTCCGTTG	CTGTTTTTTT	ATAAACACAC	TCCTTGGAAG	AAAAAAAAAA	AAAAAAAAAA
1390	1400	1410	1420	1430	1440
AAA.....

Figure 4

10	20	30	40	50
GGAGCGAGCTGGCGGCGCGCGCTCGGGCGCGCGCGGGGCC	ATG	GAG	CTG	TGG
	Met	Glu	Leu	Trp
				Pro
60	70	80	90	
TGT CTG GCC GCG GCG CTG CTG CTG TTG CTG CTG CTG CTG	CTG	CTG	CTG	CAG
Cys Leu Ala Ala Ala Leu Leu Leu Leu Leu Leu Leu	Val	Gln	Leu	Leu
				20
100	110	120	130	140
AGC CGC GCG GCC GAG TTC TAC GCC AAG GTC GCC CTG TAC TGC	GCG			
Ser Arg Ala Ala Ala Glu Phe Tyr Ala Lys Val Ala Leu Tyr Cys	Ala			
				30
150	160	170	180	
CTG TGC TTC ACG GTG TCC GCC GTG GCC TCG CTC TGC CTG CTG				
Leu Cys Phe Thr Val Ser Ala Val Ala Ser Leu Val Cys Leu	Leu			
				50
190	200	210	220	230
TGC CAC GGC GGC CGG ACG GTG GAG AAC ATG AGC ATC ATC GGC	TGG			
Cys His Gly Gly Arg Thr Val Glu Asn Met Ser Ile Ile Gly	Trp			
				60

Title: METHOD OF SCREENING
COMPOUNDS THAT INHIBIT
LYSOPHOSPHATIDIC ACID
ACYLTRANSFERASE

Inventors: David W. LEUNG et al.

Docket No.: 077319-0382

Figure 4 (continued)

240	250	260	270		
TTC GTG CGA AGC TTC AAG TAC TTT TAC GGG CTC CGC TTC GAG GTG					
Phe Val Arg Ser Phe Lys Tyr Phe Tyr Gly Leu Arg Phe Glu Val					80
	70				
280	290	300	310	320	
CGG GAC CCG CGC AGG CTG CAG GAG GCC CGT CCC TGT GTC ATC GTC					
Arg Asp Pro Arg Arg Leu Gln Glu Ala Arg Pro Cys Val Ile Val					
			90		
330	340	350	360		
TCC AAC CAC CAG AGC ATC CTG GAC ATG ATG GGC CTC ATG GAG GTC					
Ser Asn His Gln Ser Ile Leu Asp Met Met Gly Leu Met Glu Val					110
	100				
370	380	390	400	410	
CTT CCG GAG CGC TGC GTG CAG ATC GCC AAG CGG GAG CTC CTC TTC					
Leu Pro Glu Arg Cys Val Gln Ile Ala Lys Arg Glu Leu Leu Phe					
			120		
420	430	440	450		
CTG GGG CCC GTG GGC CTC ATC ATG TAC CTC GGG GGC GTC TTC TTC					
Leu Gly Pro Val Gly Leu Ile Met Tyr Leu Gly Gly Val Phe Phe					140
	130				
460	470	480	490	500	
ATC AAC CCG CAG CGC TCT AGC ACT GCC ATG ACA GTG ATG GCC GAC					
Ile Asn Arg Gln Arg Ser Ser Thr Ala Met Thr Val Met Ala Asp					
					150

Figure 4 (continued)

510	520	530	540
CTG GGC GAG CGC ATG GTC AGG GAG AAC CTC AAA GTG TGG ATC TAT			
Leu Gly Glu Arg Met Val Arg Glu Asn Leu Lys Val Trp Ile Tyr			
160			170
550	560	570	580
CCC GAG GGT ACT CGC AAC GAC AAT GGG GAC CTG CTG CCT TTT AAG			
Pro Glu Gly Thr Arg Asn Asp Asn Gly Asp Leu Leu Pro Phe Lys			
			180
600	610	620	630
AAG GGC GCC TTC TAC CTG GCA GTC CAG GCA CAG GTG CCC ATC GTC			
Lys Gly Ala Phe Tyr Leu Ala Val Gln Ala Gln Val Pro Ile Val			
	190		200
640	650	660	670
CCC GTG GTG TAC TCT TCC TTC TCC TCC TTC TAC AAC ACC AAG AAG			
Pro Val Val Tyr Ser Ser Phe Ser Ser Phe Tyr Asn Thr Lys Lys			
			210
690	700	710	720
AAG TTC TTC ACT TCA GGA ACA GTC ACA GTG CAG GTG CTG GAA GCC			
Lys Phe Phe Thr Ser Gly Thr Val Thr Val Gln Val Leu Glu Ala			
			220
			230

Figure 4 (continued)

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730          740          750          760          770
ATC CCC ACC AGC GGC CTC ACT GCG GCG GAC GTC CCT GCG CTC GTG
Ile Pro Thr Ser Gly Leu Thr Ala Ala Asp Val Pro Ala Leu Val
240

780          790          800          810
GAC ACC TGC CAC CCG GCC ATG AGG ACC ACC TTC CTC CAC ATC TCC
Asp Thr Cys His Arg Ala Met Arg Thr Thr Phe Leu His Ile Ser
250

820          830          840          850          860
AAG ACC CCC CAG GAG AAC GGG GCC ACT GCG GGG TCT GGC GTG CAG
Lys Thr Pro Gln Glu Asn Gly Ala Thr Ala Gly Ser Gly Val Gln
270

870          880          890          900          910          920
CCG GCC CAG TAG CCCAGACCACGGCAGGGCATGACCTGGGGAGGGCAGGTGGAAGC
Pro Ala Gln ***

930          940          950          960          970          980
CGATGGCTGGAGGATGGGCAGAGGGGACTCCTCCCGGCTTCCAATACCACCTCTGTCCGG

990          1000          1010          1020          1030          1040
CTCCCCAGCTCTCACTCAGCCCGGGAAGCAGGAAGCCCTTCTGTCTACTGGTCTCAGAC
1050          1060          1070          1080          1090          1100
ACAGGCCCCGTGTCTCCCTGCAGGGGGCTCAGCTGGACCCCTCCCCGGCTCGAGGGCAG

```

Figure 4 (continued)

1110	1120	1130	1140	1150	1160
	GGACTCGCGCC	CACGGCACCT	CTGGGNGCT	GGGNTGATA	AAGATGAGGCTTGC
	GGCTG				CGGCTGTG
1170	1180	1190	1200	1210	1220
	GCCCGCTGGT	GGCTGAGCC	ACAAGGCCCC	CGATGGCCC	CAGGAGCAGATGG
	AGACCC				AGACCC
1230	1240	1250	1260	1270	1280
	GAGGCCAGG	AGTCCCAG	ACTCACG	CACCTTGG	CCACAGGAGCCG
	GAATCGGG				CGCTG
1290	1300	1310	1320	1330	1340
	CTGCTCCT	GCTGGCCT	GAAATCT	GTGGGT	CAGCACTGTACT
	CGT				CGTGTGTTTTT
1350	1360	1370	1380		
	ATAAACAC	ACTCTTG	GAAAAA	AAAAA	AAAAA

Figure 5

Alignment of LPAAT Sequences.

Human LPAAT- β	1	10	20	30	40	50
Human LPAAT- α	1	-----	-----	<u>MEL</u> <u>WPC</u> -----	<u>LA</u> <u>AA</u> <u>LLLLLL</u> <u>V</u>	
Yeast LPAAT	1	-----	-----	<u>MDL</u> <u>WPGAWMLLL</u> <u>L</u>	<u>LFL</u> <u>LLL</u> <u>FLL</u> <u>P</u>	
E.coli LPAAT	1	-----	-----	<u>MSV</u> -- <u>IGRFL</u> <u>YYL</u>	<u>RSVL</u> <u>WL</u> <u>LA</u> <u>LA</u>	
H.influenzae	1	-----	-----	-----	-----	
S.typhimurium	1	-----	-----	-----	-----	
L.douglassi	1	<u>MAKIR</u> <u>SS</u> <u>L</u>	<u>RNR</u> -----	-----	<u>RLKP</u> <u>AVA</u> <u>TAD</u> --	<u>D</u> <u>DKDGV</u> <u>FWV</u> --
C. nucifera	1	<u>MDASG</u> <u>ASS</u> <u>FL</u>	<u>RCRCLE</u> <u>SCFK</u>	<u>ASFGMS</u> <u>QPKD</u>	<u>AAGQ</u> <u>SRPA</u>	<u>DAD</u> <u>DFIVDD</u>
Human LPAAT- β	51	<u>QL</u> -----	<u>SFAAE</u> <u>FYAK</u> <u>VAL</u> --	<u>YC</u> <u>ALCF</u> <u>TVSA</u> <u>VA</u>	<u>SLVCLL</u> <u>CHGG</u>	<u>RTVENM</u> <u>SII</u>
Human LPAAT- α	51	<u>TLWFCS</u> <u>HS</u> <u>AK</u>	<u>YFFK</u> <u>MAF</u> --	<u>YN</u> <u>GWIL</u> <u>FLA</u> <u>VLA</u>	<u>IPVCA</u> <u>V</u> --	<u>RG</u> <u>RNVENM</u> <u>KIL</u>
Yeast LPAAT	51	<u>G</u> --- <u>CG</u> ---	<u>FY</u> -----	-----	<u>GVIA</u> <u>SILCT</u> <u>LICKQ</u>	<u>HLAQMI</u> <u>TAR</u>
E.coli LPAAT	51	-----	<u>MLYI</u> <u>FR</u> <u>LIT</u> <u>VIYS</u>	<u>ILVC</u> --- <u>VFG</u>	<u>SIYCL</u> <u>FS</u> <u>PRN</u>	<u>PKHV</u> --- <u>ATF</u>
H.influenzae	51	-----	<u>MLKL</u> <u>LRI</u> <u>FLML</u> <u>IOC</u>	<u>ILIC</u> --- <u>VLG</u>	<u>TIYSFIRE</u> <u>KN</u>	<u>PSNV</u> --- <u>GIV</u>
S.typhimurium	51	-----	<u>MLYI</u> <u>FR</u> <u>LIV</u> <u>TVIYS</u>	<u>ILVC</u> --- <u>VFG</u>	<u>SIYCL</u> <u>FS</u> <u>PRN</u>	<u>PKHV</u> --- <u>ATF</u>
L.douglassi	51	-----	<u>LLSC</u> <u>FKIF</u> <u>VCF</u> <u>AFT</u>	<u>WLI</u> <u>TAV</u> <u>AWG</u>	<u>LIM</u> <u>LLP</u> <u>WP</u>	<u>YMRIR</u> <u>LG</u> <u>NY</u>
C. nucifera	51	<u>DRWT</u> <u>VI</u> <u>LSV</u>	<u>VRI</u> <u>AAC</u> <u>FL</u> --	<u>SNM</u> <u>TTI</u> <u>VVN</u>	<u>MIM</u> <u>ILL</u> <u>PWP</u>	<u>YARIR</u> <u>Q</u> <u>GNLY</u>

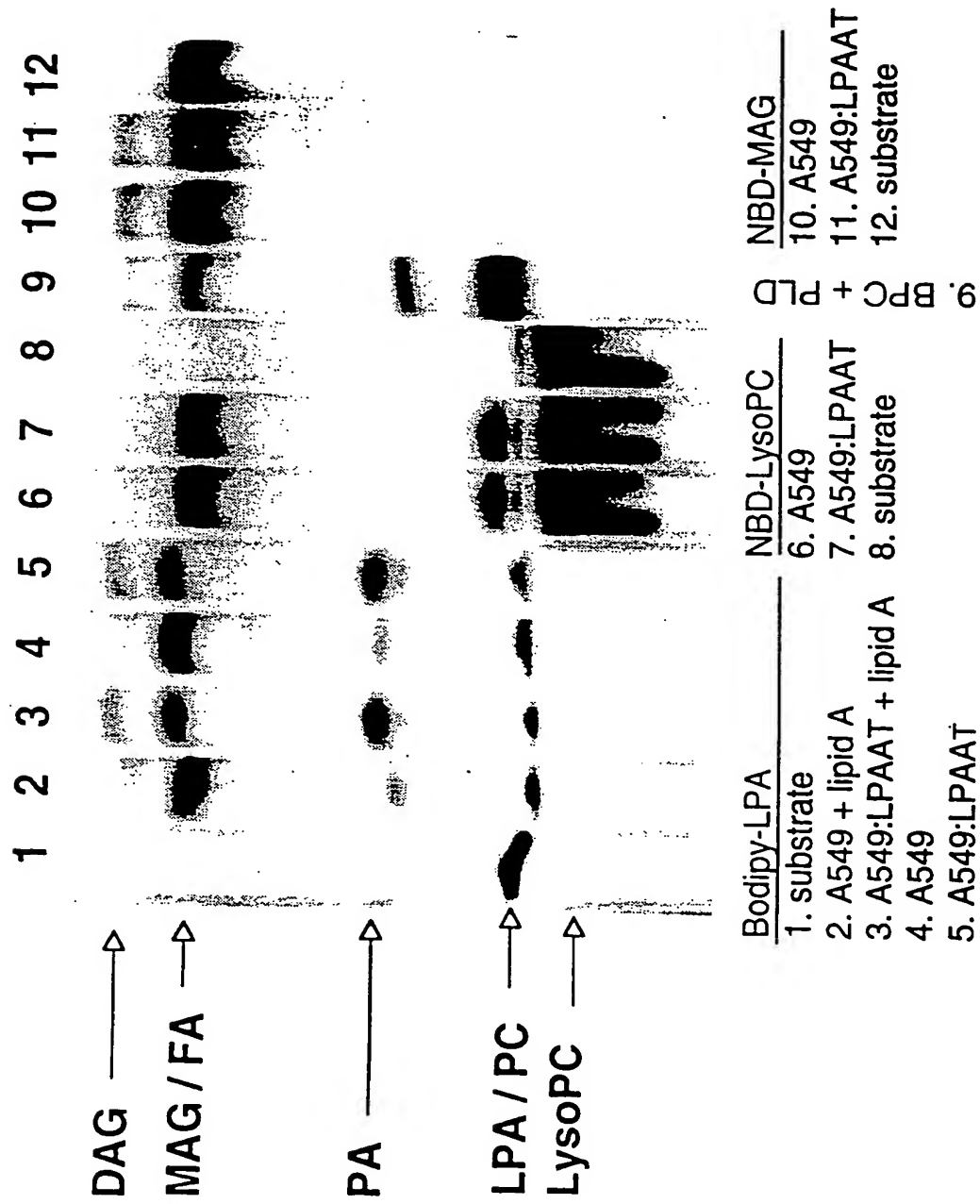
Figure 5 (continued)

Human LPAAT- β	101	<u>GW</u> <u>FV</u> <u>RS</u> <u>F</u> <u>KY</u> - -- <u>FY</u> <u>GL</u> <u>RF</u> <u>EV</u> <u>RD</u> <u>PR</u> <u>RL</u> <u>Q</u> <u>EAR</u> <u>PC</u> <u>V</u> <u>I</u> <u>V</u> <u>SN</u> <u>HQ</u> <u>S</u> <u>I</u> <u>L</u> <u>DM</u> <u>GI</u> <u>MEV</u>	110	120	130	140	150
Human LPAAT- α	101	<u>RL</u> <u>ML</u> <u>I</u> <u>HI</u> <u>KY</u> - -- <u>LY</u> <u>G</u> <u>IR</u> <u>VEV</u> <u>RG</u> <u>AH</u> <u>F</u> <u>PP</u> <u>SQ</u> <u>PY</u> <u>VV</u> <u>SN</u> <u>HQ</u> <u>S</u> <u>SL</u> <u>DL</u> <u>IG</u> <u>MEV</u>					
Yeast LPAAT	101	<u>CFY</u> - <u>HVM</u> <u>KL</u> - -- <u>ML</u> <u>GL</u> <u>DV</u> <u>KV</u> <u>VGE</u> <u>EN</u> <u>AK</u> - <u>K</u> <u>PY</u> <u>IM</u> <u>IAN</u> <u>HQ</u> <u>S</u> <u>TLD</u> <u>IF</u> <u>ML</u> <u>GRI</u>					
E.coli LPAAT	101	<u>GHM</u> <u>F</u> <u>GRL</u> --- <u>AP</u> <u>LF</u> <u>GL</u> <u>K</u> <u>VE</u> <u>C</u> <u>RK</u> <u>PT</u> <u>DA</u> <u>ES</u> <u>YG</u> <u>NA</u> <u>IY</u> <u>IAN</u> <u>HQ</u> <u>N</u> <u>NY</u> <u>DM</u> <u>VT</u> <u>A</u> <u>SNI</u>					
H.influenzae	101	<u>ARW</u> <u>F</u> <u>GRL</u> - <u>FT</u> <u>YPL</u> <u>F</u> <u>GL</u> <u>K</u> <u>VEH</u> <u>RI</u> <u>PQ</u> <u>DQ</u> <u>KQ</u> <u>IS</u> <u>RA</u> <u>IY</u> <u>IGN</u> <u>HQ</u> <u>N</u> <u>NY</u> <u>DM</u> <u>VT</u> <u>ISYM</u>					
S.typhimurii	101	<u>GHM</u> <u>F</u> <u>GRL</u> - <u>FT</u> <u>AP</u> <u>LF</u> <u>GL</u> <u>K</u> <u>VE</u> <u>C</u> <u>RK</u> <u>PA</u> <u>DA</u> <u>EN</u> <u>YG</u> <u>NA</u> <u>IY</u> <u>IAN</u> <u>HQ</u> <u>N</u> <u>NY</u> <u>DM</u> <u>VT</u> <u>A</u> <u>NI</u>					
L.douglassi	101	<u>GH</u> <u>I</u> <u>IG</u> <u>LV</u> -- <u>IW</u> <u>YG</u> <u>I</u> <u>PI</u> <u>KI</u> <u>QG</u> <u>SE</u> <u>HI</u> <u>K</u> <u>KRA</u> <u>IFT</u> <u>Y</u> <u>I</u> <u>SN</u> <u>HAS</u> <u>PI</u> <u>DA</u> <u>FF</u> <u>V</u> <u>MWL</u>					
C. nucifera	101	<u>GHV</u> <u>T</u> <u>GR</u> <u>M</u> <u>FT</u> <u>MW</u> <u>IL</u> <u>GN</u> <u>PT</u> <u>TI</u> <u>EG</u> <u>SE</u> <u>FS</u> <u>N</u> <u>T</u> <u>RA</u> <u>I</u> -- <u>YI</u> <u>CN</u> <u>HAS</u> <u>LVD</u> <u>IF</u> <u>LI</u> <u>MWL</u>					
Human LPAAT- β	151	<u>LP</u> <u>ER</u> <u>CV</u> <u>Q</u> <u>IAK</u> <u>RE</u> <u>LL</u> <u>FL</u> <u>GPV</u> - - <u>GL</u> <u>IM</u> <u>Y</u> <u>LCV</u> <u>FF</u> <u>IN</u> <u>RQ</u> <u>RS</u> <u>ST</u> <u>AM</u> <u>T</u> -- <u>VM</u> <u>ADL</u>	160	170	180	190	200
Human LPAAT- α	151	<u>LP</u> <u>G</u> <u>RCV</u> <u>P</u> <u>IAK</u> <u>RE</u> <u>LL</u> <u>W</u> <u>AGSA</u> - - <u>GL</u> <u>AC</u> <u>WL</u> <u>AGV</u> <u>I</u> <u>F</u> <u>IDR</u> <u>KR</u> <u>IGD</u> <u>AI</u> <u>S</u> -- <u>VM</u> <u>SEV</u>					
Yeast LPAAT	151	<u>FPP</u> <u>GC</u> <u>IV</u> <u>TAK</u> <u>KSL</u> <u>KV</u> <u>VP</u> <u>FL</u> - - <u>GW</u> <u>F</u> <u>MA</u> <u>LSGT</u> <u>Y</u> <u>F</u> <u>LDR</u> <u>SKRQ</u> <u>E</u> <u>AI</u> <u>D</u> -- <u>T</u> <u>INKG</u>					
E.coli LPAAT	151	<u>VQP</u> <u>PTV</u> <u>TVGK</u> <u>KSL</u> <u>LW</u> <u>IPFF</u> - - <u>GQ</u> <u>LY</u> <u>WL</u> <u>TGN</u> <u>LL</u> <u>IDR</u> <u>NNR</u> <u>TK</u> <u>AH</u> <u>G</u> -- <u>T</u> <u>IAEV</u>					
H.influenzae	151	<u>VQP</u> <u>RTV</u> <u>SVGK</u> <u>KSL</u> <u>IW</u> <u>IPFF</u> <u>F</u> <u>TG</u> <u>ILY</u> <u>WV</u> <u>VTGN</u> <u>I</u> <u>F</u> <u>LDR</u> <u>ENR</u> <u>TK</u> <u>AH</u> <u>N</u> -- <u>T</u> <u>MSQL</u>					
S.typhimurii	151	<u>VQP</u> <u>PTV</u> <u>TVGK</u> <u>KSL</u> <u>LW</u> <u>IPFF</u> <u>F</u> <u>TG</u> <u>Q</u> <u>LY</u> <u>WL</u> <u>TGN</u> <u>LL</u> <u>IDR</u> <u>NNR</u> <u>AK</u> <u>AH</u> <u>S</u> -- <u>T</u> <u>IAAV</u>					
L.douglassi	151	<u>AP</u> <u>IG</u> <u>IV</u> <u>GVAK</u> <u>KE</u> <u>VI</u> <u>W</u> <u>YP</u> <u>ILG</u> <u>Q</u> -- <u>LY</u> <u>T</u> <u>LAH</u> <u>I</u> <u>R</u> <u>IDR</u> <u>SN</u> <u>PAA</u> <u>AI</u> <u>QS</u> <u>FT</u> <u>MKEA</u>					
C. nucifera	151	<u>IP</u> <u>GT</u> <u>IV</u> <u>IAK</u> <u>KE</u> <u>II</u> <u>W</u> <u>Y</u> <u>PL</u> <u>FG</u> <u>Q</u> <u>FT</u> <u>LY</u> <u>V</u> <u>LANH</u> <u>Q</u> <u>R</u> <u>IDR</u> <u>SN</u> <u>P</u> <u>SA</u> <u>AI</u> <u>ES</u> -- <u>I</u> <u>KEV</u>					

Figure 5 (continued)

	310	320	330	340	350
Human LPAAT- β	301 <u>AMRTTFLHIS</u>	<u>KTPQENGATA</u>	<u>GSGVQPAQ*</u>	-----	-----
Human LPAAT- α	301 <u>SMLTTFREIS</u>	<u>TDGRGGDYL</u>	<u>KPGGGG*</u>	-----	-----
Yeast LPAAT	301 <u>QMVDILKEIG</u>	<u>YSPAINDTTL</u>	<u>PPQAIEYAAL</u>	<u>QHDKKVNNKI</u>	<u>KNEPVPSVSI</u>
E.coli LPAAT	301 <u>-SIMEQKIAE</u>	<u>LDKEVA-ER</u>	<u>EAAGKV*</u>	-----	-----
H.influenzae	301 <u>TILMEKRIAE</u>	<u>LDEEIA</u>	-----	<u>KGK*</u>	-----
S.typhimurii	301 <u>TALMEQKIAE</u>	<u>LDKEVA-ER</u>	<u>EATGKV*</u>	-----	-----
L.douglassi	301 <u>IYVRNLPASQ</u>	<u>KPLGS--TNR</u>	<u>--S-K*</u>	-----	-----
C. nucifera	301 <u>TALYVDHLPE</u>	<u>SQKPLVSKGR</u>	<u>DASGRNS*</u>	-----	-----
	360	370	380	390	
Human LPAAT- β	351 -----	-----	-----	-----	-----
Human LPAAT- α	351 -----	-----	-----	-----	-----
Yeast LPAAT	351 <u>SNDVNIHNEG</u>	<u>SSVKKMH*</u>	-----	-----	-----
E.coli LPAAT	351 -----	-----	-----	-----	-----
H.influenzae	351 -----	-----	-----	-----	-----
S.typhimurii	351 -----	-----	-----	-----	-----
L.douglassi	351 -----	-----	-----	-----	-----
C. nucifera	351 -----	-----	-----	-----	-----

Figure 6



TLC Analysis of Acyltransferase Activity

Title: METHOD OF SCREENING
COMPOUNDS THAT INHIBIT
LYSOPHOSPHATIDIC ACID
ACYLTRANSFERASE

Inventors: David W. LEUNG et al.

Docket No.: 077319-0382

Induction of TNF in A549 LPAAT or A549
cells stimulated with mTNF and IL-1

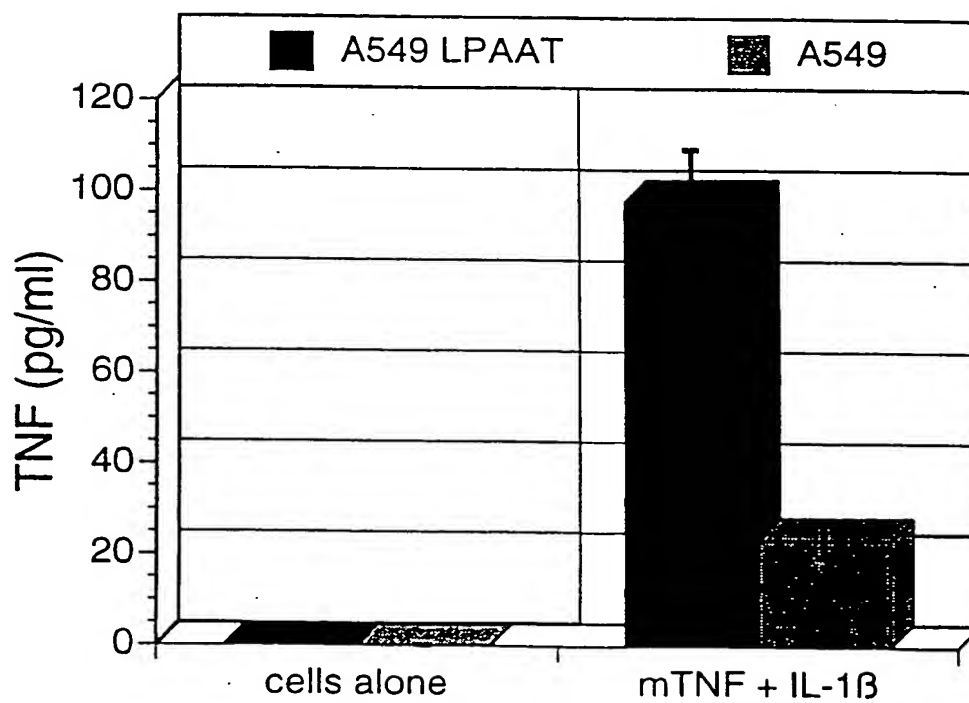


Figure 7

**Induction of IL-6 in A549 LPAAT or A549
cells stimulated with mTNF and IL-1**

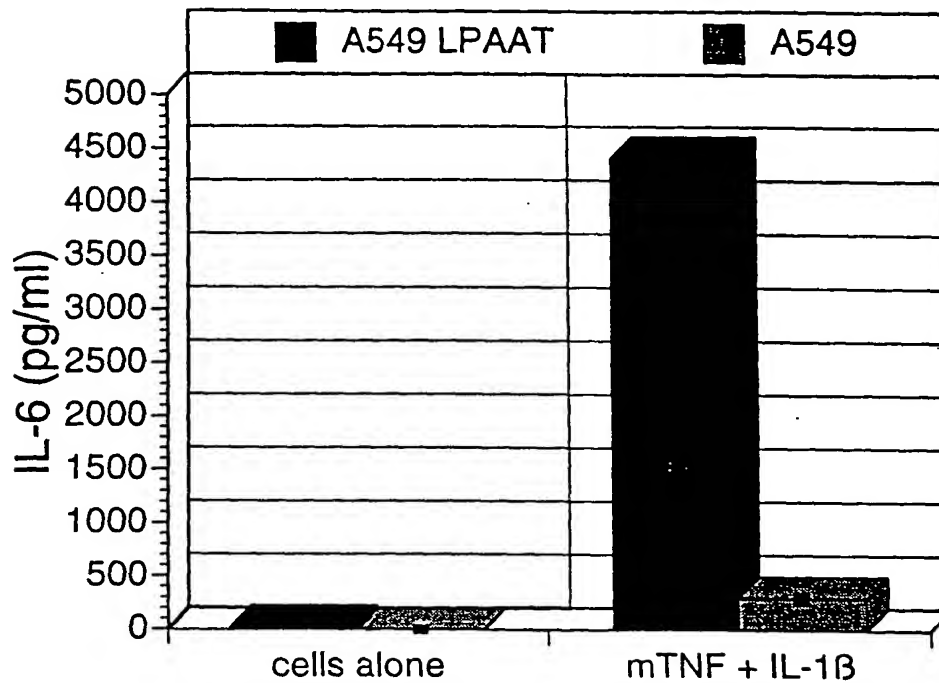


Figure 8

Title: METHOD OF SCREENING
COMPOUNDS THAT INHIBIT
LYSOPHOSPHATIDIC ACID
ACYLTRANSFERASE

Inventors: David W. LEUNG et al.

Docket No.: 077319-0382

Figure 9 Translated sequence of human LPAAT-yl

TCTATGAAACCAACATACATGGCGTTTGCATCACAGTTGGAGTCAGATGTGAGCCCGGAG	60
GGCAGGTGTCTGGCTTGTCCACCCGGAAGCCCTGAGGGCAGCTGTTCCCACTGGCTCTGC	120
TGACCTTGTGCCTTGGACGGCTGTCCTCAGCGAGGGGCCGTGCACCCGCTCCTGAGCAGC	180
GCC <u>ATG</u> GGC CTG CTG GCC TTC CTG AAG ACC CAG TTC GTG CTG CAC	225
Met Gly Leu Leu Ala Phe Leu Lys Thr Gln Phe Val Leu His	
5 10	
CTG CTG GTC GGC TTT GTC TTC GTG GTG AGT GGT CTG GTC ATC AAC	270
Leu Leu Val Gly Phe Val Phe Val Val Ser Gly Leu Val Ile Asn	
15 20 25	
TTC GTC CAG CTG TGC ACG CTG GCG CTC TGG CCG GTC AGC AAG CAG	315
Phe Val Gln Leu Cys Thr Leu Ala Leu Trp Pro Val Ser Lys Gln	
30 35 40	
CTC TAC CGC CGC CTC AAC TGC CGC CTC GCA TAC TCA CTC TGG AGC	360
Leu Tyr Arg Arg Leu Asn Cys Arg Leu Ala Tyr Ser Leu Trp Ser	
45 50 55	
CAA CTG GTC ATG CTG CTG GAG TGG TGG TCC TGC ACG GAG TGT ACA	405
Gln Leu Val Met Leu Leu Glu Trp Trp Ser Cys Thr Glu Cys Thr	
60 65 70	
CTG TTC ACG GAC CAG GCC ACG GTA GAG CGC TTT GGG AAG GAG CAC	450
Leu Phe Thr Asp Gln Ala Thr Val Glu Arg Phe Gly Lys Glu His	
75 80 85	
GCA GTC ATC ATC CTC AAC CAC AAC TTC GAG ATC GAC TTC CTC TGT	495
Ala Val Ile Ile Leu Asn His Asn Phe Glu Ile Asp Phe Leu Cys	
90 95 100	
GGG TGG ACC ATG TGT GAG CGC TTC GGA GTG CTG GGG AGC TCC AAG	540
Gly Trp Thr Met Cys Glu Arg Phe Gly Val Leu Gly Ser Ser Lys	
105 110 115	
GTC CTC GCT AAG AAG GAG CTG CTC TAC GTG CCC CTC ATC GGC TGG	585
Val Leu Ala Lys Lys Glu Leu Leu Tyr Val Pro Leu Ile Gly Trp	
120 125 130	
ACG TGG TAC TTT CTG GAG ATT GTG TTC TGC AAG CGG AAG TGG GAG	630
Thr Trp Tyr Phe Leu Glu Ile Val Phe Cys Lys Arg Lys Trp Glu	
135 140 145	
GAG GAC CGG GAC ACC GTG GTC GAA GGG CTG AGG CGC CTG TCG GAC	675
Glu Asp Arg Asp Thr Val Val Glu Gly Leu Arg Arg Leu Ser Asp	
150 155 160	
TAC CCC GAG TAC ATG TGG TTT CTC CTG TAC TGC GAG GGG ACG CGC	720
Tyr Pro Glu Tyr Met Trp Phe Leu Leu Tyr Cys Glu Gly Thr Arg	
165 170 175	
TTC ACG GAG ACC AAG CAC CGC GTT AGC ATG GAG GTG GCG GCT GCT	765
Phe Thr Glu Thr Lys His Arg Val Ser Met Glu Val Ala Ala Ala	
180 185 190	
AAG GGG CTT CCT GTC CTC AAG TAC CAC CTG CTG CCG CGG ACC AAG	810
Lys Gly Leu Pro Val Leu Lys Tyr His Leu Leu Pro Arg Thr Lys	
195 200 205	
GGC TTC ACC ACC GCA GTC AAG TGC CTC CGG GGG ACA GTC GCA GCT	855
Gly Phe Thr Thr Ala Val Lys Cys Leu Arg Gly Thr Val Ala Ala	
210 215 220	
GTC TAT GAT GTA ACC CTG AAC TTC AGA GGA AAC AAG AAC CCG TCC	900
Val Tyr Asp Val Thr Leu Asn Phe Arg Gly Asn Lys Asn Pro Ser	
225 230 235	
CTG CTG GGG ATC CTC TAC GGG AAG AAG TAC GAG GCG GAC ATG TGC	945
Leu Leu Gly Ile Leu Tyr Gly Lys Lys Tyr Glu Ala Asp Met Cys	
240 245 250	
GTG AGG AGA TTT CCT CTG GAA GAC ATC CCG CTG GAT GAA AAG GAA	990
Val Arg Arg Phe Pro Leu Glu Asp Ile Pro Leu Asp Glu Lys Glu	
255 260 265	
GCA GCT CAG TGG CTT CAT AAA CTG TAC CAG GAG AAG GAC GCG CTC	1035

Title: METHOD OF SCREENING
COMPOUNDS THAT INHIBIT
LYSOPHOSPHATIDIC ACID
ACYLTRANSFERASE

Inventors: David W. LEUNG et al.

Docket No.: 077319-0382

Figure 9 (continued)

Ala	Ala	Gln	Trp	Leu	His	Lys	Leu	Tyr	Gln	Glu	Lys	Asp	Ala	Leu	
270					275					280					
CAG	GAG	ATA	TAT	AAT	CAG	AAG	GGC	ATG	TTT	CCA	GGG	GAG	CAG	TTT	1080
Gln	Glu	Ile	Tyr	Asn	Gln	Lys	Gly	Met	Phe	Pro	Gly	Glu	Gln	Phe	
285					290					295					
AAG	CCT	GCC	CGG	AGG	CCG	TGG	ACC	CTC	CTG	AAC	TTC	CTG	TCC	TGG	1125
Lys	Pro	Ala	Arg	Arg	Pro	Trp	Thr	Leu	Leu	Asn	Phe	Leu	Ser	Trp	
300					305					310					
GCC	ACC	ATT	CTC	CTG	TCT	CCC	CTC	TTC	AGT	TTT	GTC	TTG	GGC	GTC	1170
Ala	Thr	Ile	Leu	Leu	Ser	Pro	Leu	Phe	Ser	Phe	Val	Leu	Gly	Val	
315					320					325					
TTT	GCC	AGC	GGA	TCA	CCT	CTC	CTG	ATC	CTG	ACT	TTC	TTG	GGG	TTT	1215
Phe	Ala	Ser	Gly	Ser	Pro	Leu	Leu	Ile	Leu	Thr	Phe	Leu	Gly	Phe	
330					335					340					
GTG	GGA	GCA	GCT	TCC	TTT	GGA	GTT	CGC	AGA	CTG	ATA	GGA	GTA	ACT	1260
Val	Gly	Ala	Ala	Ser	Phe	Gly	Val	Arg	Arg	Leu	Ile	Gly	Val	Thr	
345					350					355					
GAG	ATA	GAA	AAA	GGC	TCC	AGC	TAC	GGA	AAC	CAA	GAG	TTT	AAG	AAA	1305
Glu	Ile	Glu	Lys	Gly	Ser	Ser	Tyr	Gly	Asn	Gln	Glu	Phe	Lys	Lys	
360					365					370					
AAG	GAA	TAA	TTA	TGG	CTGTG	ACTGA	ACAC	ACG	CGCC	CTGAC	GGTGG	TATCC	AGTT		1362
Lys	Glu	***													
AACTCAA	AAACCA	CACAC	AGAGT	GCAGG	AAAA	GACA	ATTAG	AACTAT	TTTTT	CTTAT	TAA				1422
CTGGT	ACTAAT	ATTAACA	AACTT	GAGCCA	AGAGTAA	AGAATTC	AGAAGGC	CTGTC	AGG						1482
TGAAGT	CTTCAG	CCTCCC	CACAG	CGCAGGGT	CCCAG	CATCTCC	ACGCG	CGCCCG	TGGGAGG						1542
TGGGT	CCGCGG	AGAGG	CCTCCC	CGGAC	GCCGTCT	CTCCAG	AACTCC	GCTTCCA	AGAG						1602
GGACCT	TTGGCT	GCTTT	CTCTC	CTTAA	ACTTAG	ATCAA	ATTTT	AAAAAAAA							1660

Title: METHOD OF SCREENING
COMPOUNDS THAT INHIBIT
LYSOPHOSPHATIDIC ACID
ACYLTRANSFERASE

Inventors: David W. LEUNG et al.

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Figure 10 Translated sequence of LPAAT-γ2 cDNA

CACGCTGGCGCTCTGGCCGGTCAGCAAGCAGCTCTACCGCCGCTCAACTGCCGCTCGCC	61
TACTCACTCTGGAGCCTAGCACAACTAGAAAGCAACCCAAGCACCTGTCACTGGAGACT	121
AATTATGCGGCACCCATACAGGGACCCTCTGCGGCCATCATGGAGAGCCTTCATCTTGCC	181
CGTACAGTTTAAAGCGAAAAAGGAAGTATACAACAAAGTCCATAACTGGTC	238
Met Leu	
CTG GAG TGG TGG TCC TGC ACG GAG TGT ACA CTG TTC ACG GAC CAG	283
Leu Glu Trp Trp Ser Cys Thr Glu Cys Thr Leu Phe Thr Asp Gln	
5 10 15	
GCC ACG GTA GAG CGC TTT GGG AAG GAG CAC GCA GTC ATC ATC CTC	328
Ala Thr Val Glu Arg Phe Gly Lys Glu His Ala Val Ile Ile Leu	
20 25 30	
AAC CAC AAC TTC GAG ATC GAC TTC CTC TGT GGG TGG ACC ATG TGT	373
Asn His Asn Phe Glu Ile Asp Phe Leu Cys Gly Trp Thr Met Cys	
35 40 45	
GAG CGC TTC GGA GTG CTG GGG AGC TCC AAG GTC CTC GCT AAG AAG	418
Glu Arg Phe Gly Val Leu Gly Ser Ser Lys Val Leu Ala Lys Lys	
50 55 60	
GAG CTG CTC TAC GTG CCC CTC ATC GGC TGG ACG TGG TAC TTT CTG	463
Glu Leu Leu Tyr Val Pro Leu Ile Gly Trp Thr Trp Tyr Phe Leu	
65 70 75	
GAG ATT GTG TTC TGC AAG CGG AAG TGG GAG GAG GAC CGG GAC ACC	508
Glu Ile Val Phe Cys Lys Arg Lys Trp Glu Glu Asp Arg Asp Thr	
80 85 90	
GTG GTC GAA GGG CTG AGG CGC CTG TCG GAC TAC CCC GAG TAC ATG	553
Val Val Glu Gly Leu Arg Arg Leu Ser Asp Tyr Pro Glu Tyr Met	
95 100 105	
TGG TTT CTC CTG TAC TGC GAG GGG ACG CGC TTC ACG GAG ACC AAG	598
Trp Phe Leu Leu Tyr Cys Glu Gly Thr Arg Phe Thr Glu Thr Lys	
110 115 120	
CAC CGC GTT AGC ATG GAG GTG GCG GCT GCT AAG GGG CTT CCT GTC	643
His Arg Val Ser Met Glu Val Ala Ala Ala Lys Gly Leu Pro Val	
125 130 135	
CTC AAG TAC CAC CTG CTG CCG CGG ACC AAG GGC TTC ACC ACC GCA	688
Leu Lys Tyr His Leu Leu Pro Arg Thr Lys Gly Phe Thr Thr Ala	
140 145 150	
GTC AAG TGC CTC CGG GGG ACA GTC GCA GCT GTC TAT GAT GTA ACC	733
Val Lys Cys Leu Arg Gly Thr Val Ala Ala Val Tyr Asp Val Thr	
155 160 165	
CTG AAC TTC AGA GGA AAC AAG AAC CCG TCC CTG CTG GGG ATC CTC	778
Leu Asn Phe Arg Gly Asn Lys Asn Pro Ser Leu Leu Gly Ile Leu	
170 175 180	
TAC GGG AAG AAG TAC GAG GCG GAC ATG TGC GTG AGG AGA TTT CCT	823
Tyr Gly Lys Lys Tyr Glu Ala Asp Met Cys Val Arg Arg Phe Pro	
185 190 195	
CTG GAA GAC ATC CCG CTG GAT GAA AAG GAA GCA GCT CAG TGG CTT	868
Leu Glu Asp Ile Pro Leu Asp Glu Lys Glu Ala Ala Gln Trp Leu	
200 205 210	
CAT AAA CTG TAC CAG GAG AAG GAC GCG CTC CAG GAG ATA TAT AAT	913
His Lys Leu Tyr Gln Glu Lys Asp Ala Leu Gln Glu Ile Tyr Asn	
215 220 225	
CAG AAG GGC ATG TTT CCA GGG GAG CAG TTT AAG CCT GCC CGG AGG	958
Gln Lys Gly Met Phe Pro Gly Glu Gln Phe Lys Pro Ala Arg Arg	
230 235 240	
CCG TGG ACC CTC CTG AAC TTC CTG TCC TGG GCC ACC ATT CTC CTG	1003
Pro Trp Thr Leu Leu Asn Phe Leu Ser Trp Ala Thr Ile Leu Leu	
245 250 255	
TCT CCC CTC TTC AGT TTT GTC TTG GGC GTC TTT GCC AGC GGA TCA	1048
Ser Pro Leu Phe Ser Phe Val Leu Gly Val Phe Ala Ser Gly Ser	

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Figure 10 (continued)

260	265	270	
CCT CTC CTG ATC CTG ACT TTC TTG GGG TTT GTG GGA GCA GCT TCC			1093
Pro Leu Leu Ile Leu Thr Phe Leu Gly Phe Val Gly Ala Ala Ser			
275	280	285	
TTT GGA GTT CGC AGA CTG ATA GGA GTA ACT GAG ATA GAA AAA GGC			1138
Phe Gly Val Arg Arg Leu Ile Gly Val Thr Glu Ile Glu Lys Gly			
290	295	300	
TCC AGC TAC GGA AAC CAA GAG TTT AAG AAA AAG GAA TAA TTAATGGC			1185
Ser Ser Tyr Gly Asn Gln Glu Phe Lys Lys Lys Glu ***			
305	310		
TGTGACTGAACACACGCGGCCCTGACGGTGGTATCCAGTTAACTCAAAACCAACACACAG			1245
AGTGCAGGAAAAGACAATTAGAACTATTTTTCTTATTAAGTGGTGACTAATATTAACAA			1305
AACTTGAGCCAAGAGTAAAGAATTCAGAAGGCCTGTCAGGTGAAGTCTTCAGCCTCCAC			1365
AGCGCAGGGTCCAGCATCTCCACGCGCGCCCGTGGGAGGTGGGTCCGGCCGGAGAGGCC			1425
TCCCGCGGACGCCGTCTCTCCAGAACTCCGCTTCCAAGAGGGACCTTTGGCTGCTTTCTC			1485
TCCTTAACTTAGATCAAATTTTAAAAAAAAAAAAAAAAA			1523

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TGAACCCAGCCGGCTCCATCTCAGCTTCTGGTTTCTAAGTCCATGTGCCAAAGGCTGCCAG															61
GAAGGAGACGCCTTCCTGAGTCCTGGATCTTTCTTCCCTTCTGGAAATCTTTGACTGTGGG															121
TAGTTATTTATTTCTGAATAAGAGCGTCCACGCATC															175
Met Asp Leu Ala Gly Leu															
5															
CTG	AAG	TCT	CAG	TTC	CTG	TGC	CAC	CTG	GTC	TTC	TGC	TAC	GTC	TTT	220
Leu	Lys	Ser	Gln	Phe	Leu	Cys	His	Leu	Val	Phe	Cys	Tyr	Val	Phe	
10															
15															
ATT	GCC	TCA	GGG	CTA	ATC	ATC	AAC	ACC	ATT	CAG	CTC	TTC	ACT	CTC	265
Ile	Ala	Ser	Gly	Leu	Ile	Ile	Asn	Thr	Ile	Gln	Leu	Phe	Thr	Leu	
25															
30															
CTC	CTC	TGG	CCC	ATT	AAC	AAG	CAG	CTC	TTC	CGG	AAG	ATC	AAC	TGC	310
Leu	Leu	Trp	Pro	Ile	Asn	Lys	Gln	Leu	Phe	Arg	Lys	Ile	Asn	Cys	
40															
45															
AGA	CTG	TCC	TAT	TGC	ATC	TCA	AGC	CAG	CTG	GTG	ATG	CTG	CTG	GAG	355
Arg	Leu	Ser	Tyr	Cys	Ile	Ser	Ser	Gln	Leu	Val	Met	Leu	Leu	Glu	
55															
60															
TGG	TGG	TCG	GGC	ACG	GAA	TGC	ACC	ATC	TTC	ACG	GAC	CCG	CGC	GCC	400
Trp	Trp	Ser	Gly	Thr	Glu	Cys	Thr	Ile	Phe	Thr	Asp	Pro	Arg	Ala	
70															
75															
TAC	CTC	AAG	TAT	GGG	AAG	GAA	AAT	GCC	ATC	GTG	GTT	CTC	AAC	CAC	445
Tyr	Leu	Lys	Tyr	Gly	Lys	Glu	Asn	Ala	Ile	Val	Val	Leu	Asn	His	
85															
90															
AAG	TTT	GAA	ATT	GAC	TTT	CTG	TGT	GGC	TGG	AGC	CTG	TCC	GAA	CGC	490
Lys	Phe	Glu	Ile	Asp	Phe	Leu	Cys	Gly	Trp	Ser	Leu	Ser	Glu	Arg	
100															
105															
TTT	GGG	CTG	TTA	GGG	GGC	TCC	AAG	GTC	CTG	GCC	AAG	AAA	GAG	CTG	535
Phe	Gly	Leu	Leu	Gly	Gly	Ser	Lys	Val	Leu	Ala	Lys	Lys	Glu	Leu	
115															
120															
GCC	TAT	GTC	CCA	ATT	ATC	GGC	TGG	ATG	TGG	TAC	TTC	ACC	GAG	ATG	580
Ala	Tyr	Val	Pro	Ile	Ile	Gly	Trp	Met	Trp	Tyr	Phe	Thr	Glu	Met	
130															
135															
GTC	TTC	TGT	TCG	CGC	AAG	TGG	GAG	CAG	GAT	CGC	AAG	ACG	GTT	GCC	625
Val	Phe	Cys	Ser	Arg	Lys	Trp	Glu	Gln	Asp	Arg	Lys	Thr	Val	Ala	
145															
150															
ACC	AGT	TTG	CAG	CAC	CTC	CGG	GAC	TAC	CCC	GAG	AAG	TAT	TTT	TTC	670
Thr	Ser	Leu	Gln	His	Leu	Arg	Asp	Tyr	Pro	Glu	Lys	Tyr	Phe	Phe	
160															
165															
CTG	ATT	CAC	TGT	GAG	GGC	ACA	CGG	TTC	ACG	GAG	AAG	AAG	CAT	GAG	715
Leu	Ile	His	Cys	Glu	Gly	Thr	Arg	Phe	Thr	Glu	Lys	Lys	His	Glu	
175															
180															
ATC	AGC	ATG	CAG	GTG	GCC	CGG	GCC	AAG	GGG	CTG	CCT	CGC	CTC	AAG	760
Ile	Ser	Met	Gln	Val	Ala	Arg	Ala	Lys	Gly	Leu	Pro	Arg	Leu	Lys	
190															
195															
CAT	CAC	CTG	TTG	CCA	CGA	ACC	AAG	GGC	TTC	GCC	ATC	ACC	GTG	AGG	805
His	His	Leu	Leu	Pro	Arg	Thr	Lys	Gly	Phe	Ala	Ile	Thr	Val	Arg	
205															
210															
AGC	TTG	AGA	AAT	GTA	GTT	TCA	GCT	GTA	TAT	GAC	TGT	ACA	CTC	AAT	850
Ser	Leu	Arg	Asn	Val	Val	Ser	Ala	Val	Tyr	Asp	Cys	Thr	Leu	Asn	
220															
225															
TTC	AGA	AAT	AAT	GAA	AAT	CCA	ACA	CTG	CTG	GGA	GTC	CTA	AAC	GGA	895
Phe	Arg	Asn	Asn	Glu	Asn	Pro	Thr	Leu	Leu						

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Figure 11 (continued)

[illegible]

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Figure 12

	10	20	30	40	50
LPAAT- γ 1	MGLLAFLKTQ	FVLHLLVGFV	FVVSGLVINP	VQ-LCTLALW	PVSKQLYRRL
LPAAT- γ 2	-----	-----	-----	-----	-----
LPAAT- δ	MDLAGLLKSQ	FLCHLVFCYV	FIASGLIINT	IQ-LFTLLW	PINKQLFRKI
	60	70	80	90	100
LPAAT- γ 1	NCRLAYSLWS	QLVMLLEWWS	CTECTLFDTQ	ATVERFGKEH	AVIILNHNFE
LPAAT- γ 2	-----	---MLLEWWS	CTECTLFDTQ	ATVERFGKEH	AVIILNHNFE
LPAAT- δ	NCRLSYCISS	QLVMLLEWWS	GTECTIFTDP	RA ³ LKYGKEN	AIVVLNHNKFE
	110	120	130	140	150
LPAAT- γ 1	IDFLCGWTMC	ERFGVLGSSK	VLAKKELLYV	PLIGWTWYFL	EIVFCRKWE
LPAAT- γ 2	IDFLCGWTMC	ERFGVLGSSK	VLAKKELLYV	PLIGWTWYFL	EIVFCRKWE
LPAAT- δ	IDFLCGWS ³ IS	ERFGLLGSSK	VLAKKELAYV	PIIGWMWYFT	EMVFCSRKWE
	160	170	180	190	200
LPAAT- γ 1	EDRDTVVEGL	RRLSDYPEYM	WFLLYCEGTR	FTETKHRVSM	EVAAAKGLPV
LPAAT- γ 2	EDRDTVVEGL	RRLSDYPEYM	WFLLYCEGTR	FTETKHRVSM	EVAAAKGLPV
LPAAT- δ	QDR ³ KT ³ VATSL	QHLRDYPEKY	FFLIHCEGTR	FTEKKHEISM	QVARAKGLPR
	210	220	230	240	250
LPAAT- γ 1	LKYHLLPRTK	GFTTAVKCLR	GTVAAYVDVT	LNF-RGNKNP	SLLGILYGKK
LPAAT- γ 2	LKYHLLPRTK	GFTTAVKCLR	GTVAAYVDVT	LNF-RGNKNP	SLLGILYGKK
LPAAT- δ	LKHLLPRTK	GFAITVRSR	NVVSAYDCT	LNF-RNNENP	³ LLGVNLGKK
	260	270	280	290	300
LPAAT- γ 1	YEADMCVRRF	PLEDIPLDEK	EAAQWLHKLY	QEKDALQEY	NQKGMFPGEQ
LPAAT- γ 2	YEADMCVRRF	PLEDIPLDEK	EAAQWLHKLY	QEKDALQEY	NQKGMFPGEQ
LPAAT- δ	YHADLYVRR	PLEDIPEDDD	EC ³ SAWLHKLY	QEKDAFQEEY	YR ³ GT ³ FP ³ ETP
	310	320	330	340	350
LPAAT- γ 1	FKPARRPWT	LNFLSWATIL	LSPLFSFVLG	VFASGSPLLI	---LTFLGFV
LPAAT- γ 2	FKPARRPWT	LNFLSWATIL	LSPLFSFVLG	VFASGSPLLI	---LTFLGFV
LPAAT- δ	MVPPRRPWT	VNWLFWAS ³ EV	LYPFFQFLVS	MIRSGSSLTL	---ASFILVF
	360	370	380		
LPAAT- γ 1	GAASFGVRR	IGVTEIEKGS	SYGNQEF--K	KKE*	
LPAAT- γ 2	GAASFGVRR	IGVTEIEKGS	SYGNQEF--K	KKE*	
LPAAT- δ	FVASVGVRW	IGVTEIDKGS	AYGNSDSKQK	LND*	

Figure 13

